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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/739,940	12/19/2000	Stephen J. Fonash	30626-101	4788
26486	7590	03/11/2004	EXAMINER	
PERKINS, SMITH & COHEN LLP ONE BEACON STREET 30TH FLOOR BOSTON, MA 02108			TRAN, MY CHAU T	
			ART UNIT	PAPER NUMBER
			1639	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/739,940	<b>Applicant(s)</b> FONASH ET AL.	
	<b>Examiner</b> MY-CHAU T TRAN	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 December 0303.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3,6,7,10-12,14-19,66,67,69,70 and 119-125 is/are pending in the application.
- 4a) Of the above claim(s) 119-124 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,6,7,10-12,14-19,66,67,69,70 and 125 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 July 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. The Examiner regrets any inconvenience to Applicant caused by the telephonic interview of 2/27/04 wherein the examiner has indicated the allowance of claims 1-3, 6-7, 10-12, 14-19, 66-67, 69-70, and 125. However on review of the amended claim 1 and search for the new limitations, a new reference was found.

### ***Status of Claims***

2. Applicant's amendment filed 12/3/03 is acknowledged and entered. Claims 1, 6-7, 10-11, 17, 66-67, and 69-70 have been amended. Claim 125 has been added. It is noted that applicant has improperly stated the status of claims 22-65 as "withdrawn" when they were canceled by the amendment filed 11/25/02 and 12/2/02.

3. In the amendment filed on 7/22/02, Claims 4, 5, 8, and 13 have been canceled and Claims 66-118 have been added.

4. Claims 9, 20-65, 68, and 71-118 have been canceled by the amendment filed on 11/25/02 and 12/2/02.

5. In the amendment filed on 6/9/03, applicant has indicated that the status of claims 22-65 as being withdrawn when the amendment filed 11/25/02 and 12/2/02 has canceled claims 22-65. Therefore, Claims 22-65 are considered canceled.

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6. In the amendment filed on 6/24/03, Claims 119-125 have been added and improperly stated the status of claims 22-65 as “withdrawn” when they were canceled by the amendment filed 11/25/02 and 12/2/02.

7. Claims 1-3, 6-7, 10-12, 14-19, 66-67, 69-70, and 119-125 are pending.

8. Claims 119-124 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

***Withdrawn Objections and /or Rejections***

9. The previous rejection under 35 USC 112, first paragraph (new matter) of claims 1-3, 6-7, 10-12, 14-19, 66-67, and 69-70 has been withdrawn in view of the amendment of claims 1, 6-7, 10-11, 17, 66-67, and 69-70.

10. The rejections under 35 USC 112, second paragraph of claims 1-3, 6-7, 10-12, 14-19, 66-67, 69-70 has been withdrawn in view of the amendment of claims 1, 6-7, 10-11, 17, 66-67, and 69-70.

11. The rejection under 35 USC 102(b) as being anticipated by Hutchens et al. (US Patent 5,719,060) for claims 1-2, 10, 12, 14, and 69-70 has been withdrawn in view of the amendment of claim 1.

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12. The rejection under 35 USC 102(e) as being anticipated by Nelson et al. (US Patent 5,955,729) for claims 1-3, 10, 12, 14, 17, 66, and 69-70 has been withdrawn in view of the amendment of claim 1.

13. The rejection under 35 USC 102(e) as being anticipated by Siuzdak et al. (US Patent 6,288,390) for claims 1-2, 6-7, 10-12, 14, 17, 66, and 69-70 has been withdrawn in view of the amendment of claim 1.

14. The rejection under 35 USC 103(a) as being unpatentable over Siuzdak et al. (US Patent 6,288,390) in view of Mian et al. (US Patent 6,319,469) for claims 1-2, 6-7, 10-12, 14, 17-19, 66-67, and 69-70 has been withdrawn in view of the amendment of claim 1.

15. The rejection under 35 USC 103(a) as being unpatentable over Siuzdak et al. (US Patent 6,288,390) in view of Farmer et al. (*J. Mass Spectrom.*, **1998**, 3:697-704) for claims 1, and 15-16 has been withdrawn in view of the amendment of claim 1.

16. Claims 1-3, 6-7, 10-12, 14-19, 66-67, 69-70, and 125 are treated on the merit in this Office Action.

***Claim Rejections - 35 USC § 102***

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3, 6-7, 10, 12, 14, 17-19, 66-67, 69-70, and 125 are rejected under 35

U.S.C. 102(b) as being anticipated by Bal et al. (*Anal. Chem.*, **1994**, 66:3423-3430).

Bal et al. disclose a method of analyzing protein by matrix-assisted laser desorption/ionization mass spectrometry (MALDI mass spectrometry) (Abstract; pg. 3423, left col., lines 1-6; pg. 3424, left col., line 45 to right col., line 17). The method comprises depositing a nafion film by evaporation onto a stainless-steel probe (metal substrate) (pg. 3425, lines 13-27) and applying the sample directly onto the nafion film after the deposition of the film (pg. 3425, left col., line 39 to right col., line 2). The nafion film is a perfluorinated cation exchanger with sulfonic acid groups (carbon hydrogen mixture) and possesses a high surface activity and can selectively bind small cations and organic cations covalently (species adsorption/analyte adsorption) (pg. 3424, left col., line 45 to right col., line 17). The protein sample is obtained by electrophoretic analysis and HPLC (pg. 3424, right col., line 50 to pg. 3425, left col., line 12; pg. 3425, lines 30-39). The sample is mix with a matrix (chemically modifying the film) (pg. 3424, right col., lines 37-49). The sample is analyzed by laser mass spectrometry (pg. 3424, right col., line 20-36).

### ***Claim Rejections - 35 USC § 103***

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

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such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. Claims 1-3, 6-7, 10-12, 14-19, 66-67, 69-70, and 125 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bal et al. (*Anal. Chem.*, **1994**, 66:3423-3430) and Farmer et al. (*J. Mass Spectrom.*, **1998**, 33:697-704).

Bal et al. disclose a method of analyzing protein by matrix-assisted laser desorption/ionization mass spectrometry (MALDI mass spectrometry) (Abstract; pg. 3423, left col., lines 1-6; pg. 3424, left col., line 45 to right col., line 17). The method comprises depositing a nafion film by evaporation onto a stainless-steel probe (metal substrate) (pg. 3425, lines 13-27) and applying the sample directly onto the nafion film after the deposition of the film (pg. 3425, left col., line 39 to right col., line 2). The nafion film is a perfluorinated cation exchanger with sulfonic acid groups (carbon hydrogen mixture) and possesses a high surface activity and can selectively bind small cations and organic cations covalently (species adsorption/analyte adsorption) (pg. 3424, left col., line 45 to right col., line 17). The protein sample is obtained by electrophoretic analysis and HPLC (pg. 3424, right col., line 50 to pg. 3425, left col., line 12; pg. 3425, lines 30-39). The sample is mix with a matrix (chemically modifying the film) (pg. 3424, right col., lines 37-49). The sample is analyzed by laser mass spectrometry (pg. 3424, right col., line 20-36)..

The method of Bal et al. does not expressly disclose enhancing the signal by using ammonium citrate as a signal enhancer.

Farmer et al. teach a method of studying protein-protein and protein-ligand interactions by mass spectrometry (pg. 697, left col. 17-19). The mass spectrometry technique is matrix-assisted laser desorption/ionization mass spectrometry (MALDI mass spectrometry). The

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method comprises dissolving both the matrix and the analytes in ammonium citrate (pg. 700, right col., lines 19-41), which provided an intense signal (pg. 700, right col., lines 42-51).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include ammonium citrate as a signal enhancer as taught by Farmer et al. in the method of Bal et al. One of ordinary skill in the art would have been motivated to include ammonium citrate as a signal enhancer in the method of Bal et al. for the advantage of providing a reagent that sequesters ions such as salt that is generally found in bimolecular analysis because the salt would form adduct peaks in a mass spectrum that compete with the peaks of the molecular ion dividing and broadening the overall signal since both Bal et al. and Farmer et al. disclose the method of analyzing protein by matrix-assisted laser desorption/ionization mass spectrometry (Bal: Abstract; Farmer: Abstract). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the method combination of Bal et al. and Farmer et al. because pH of the sample is an important factor in the detection of non-covalent complexes and changing conditions of pH and ionic strength due to solvent evaporation will affect the complex stability by disrupting inter- and intramolecular forces.

### ***Conclusion***

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct  
March 8, 2004

  
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**SUPERVISORY PATENT EXAMINER**  
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